

# Tiagabine May Reduce Bruxism and Associated Temporomandibular Joint Pain

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Tiagabine is an anticonvulsant gamma-aminobutyric acid reuptake inhibitor commonly used as an add-on treatment of refractory partial seizures in persons over 12 years old. Four of the 5 cases reported here indicate that tiagabine might also be remarkably effective in suppressing nocturnal bruxism, trismus, and consequent morning pain in the teeth, masticatory musculature, jaw, and temporomandibular joint areas. Tiagabine has a benign adverse-effect profile, is easily tolerated, and retains effectiveness over time. Bed partners of these patients report that grinding noises have stopped; therefore, the tiagabine effect is probably not simply antinociceptive. The doses used to suppress nocturnal bruxism at bedtime (4–8 mg) are lower than those used to treat seizures.

**Key Words:** Pain; Tiagabine; Bruxism; Trismus.

**B**ruuxism is the jaw clenching or grinding of teeth that usually occurs during sleep.<sup>1–5</sup> It is synonymous with trismus when referring to tonic jaw clenching, and considerable jaw pain and tooth ischemic pain in particular can be generated by this form. Lifetime occurrence of at least some orofacial pain from a night of bruxing or daytime episodes of clenching or grinding, particularly at a time of unusual stress, approaches 100%. Point prevalence is estimated at 5–10% of the adult population,<sup>5,6</sup> and a minority of these individuals develop consequent temporomandibular joint (TMJ) or orofacial pain syndromes, excessive tooth wear, or tooth fracture.<sup>7,8</sup>

Rhythmic nocturnal masticatory muscle activity in bursts of 3–5 at 1 Hz, with occlusal force generated between 3 and 80 N ( $N \approx 100$  g), is commonly seen. The relationship between the rhythmic and the tonic forms of bruxism is unclear, but both forms cause pain.<sup>2</sup> Sleep bruxism is thought to occur during microarousals or arousal transients.<sup>1,6,9</sup> Pain, TMJ structural damage, tooth damage, and nonrestorative sleep are serious consequences of bruxism for some patients and are poorly controlled by current treatments. Better bruxism treatments are needed.

Not only is bruxism more commonly a problem in individuals with depression and anxiety disorders, but also the medicines used to treat anxiety and depression can themselves often create a new iatrogenic or worsen a preexisting bruxism even when they successfully treat the target psychiatric problem.<sup>10</sup> Bruxism is more common in cerebral palsy, Down syndrome, autism, and other developmentally delayed or intellectually impaired populations. For unknown reasons, bruxism is a common mammalian response to stress; for example, rats also experience sleep bruxism during periods of stress.<sup>11</sup>

Ascription of bruxism to malocclusion and other peripheral afferent stimuli is now considered to be incorrect. Current data indicate that central primary efferents are the common and prominent drivers of bruxism.<sup>1,3,5,7,12–14</sup> For example, heart rate increases are seen just before initiation of jaw musculature contractions of a bruxism bout, and cortical electroencephalogram activity increases 4 seconds before bruxism onset.<sup>2</sup> The finding of reduced slow-wave sleep (stage III–VI) in bruxism<sup>13</sup> and its occurrence during microarousals from sleep may be relevant to tiagabine's salutary effects, as discussed below.<sup>1,5,9</sup>

## CURRENT TREATMENTS

Current first-line treatments of sleep bruxism are reviewed.<sup>15</sup> These commonly include intraoral splints and

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orthodontic correction of malocclusion. Medicines that may be provoking or exacerbating bruxism should be identified and changed if possible. (This often is not possible, as with patient MT below.)

Depression, anxiety, mood lability, or thought disorders should be sought out and corrected. One should screen for sleep apnea because it may create a secondary bruxism, and continuous positive airway pressure during sleep often results in bruxism remission when sleep apnea is comorbid.<sup>14</sup> Psychotherapy can be a useful adjunct to identify and correct psychosocial precipitants. Stopping the use of street drugs or alcohol may help. Also, careful attention to standard sleep hygiene measures (see the Appendix) may help some patients.

## TIAGABINE

Tiagabine is an anticonvulsant currently indicated by the Food and Drug Administration for add-on use in treating partial seizures.<sup>16,17</sup> Gamma-aminobutyric acid is the main central nervous system inhibitory neurotransmitter. After release into the synaptic cleft, it is taken back up into the neuron and nearby glia by several pumps specific to gamma-aminobutyric acid, one of which is termed GAT-1.<sup>18</sup> Tiagabine specifically inhibits GAT-1.<sup>16–18</sup> The adverse-effect profile of tiagabine is usually benign, with daytime tiredness being the most common effect. The only serious concern is rare induction de novo or worsening of preexisting seizures.<sup>19,20</sup> Hepatic enzyme metabolism is not altered, and concentrations of other drugs usually are not altered. However, tiagabine is metabolized by CYP3A4, and CYP3A4 inducers can alter its effectiveness. The elimination half-life is 8 hours.

Tiagabine, in addition to its approved indication, is being explored off-label for the treatment of muscle spasm and neuropathic pain,<sup>21</sup> generalized anxiety disorder,<sup>22</sup> and posttraumatic stress disorder<sup>23</sup>; for postischemic neuron protection<sup>24</sup>; for the treatment of postencephalitis impulse dyscontrol<sup>25</sup>; and for other uses.

Unique among antiseizure medicines, tiagabine increases stage III–IV sleep in humans.<sup>26</sup> Most hypnotics and modern antidepressants either reduce stages III–IV or leave them unchanged (mirtazapine is the exception; as with tiagabine, it increases stages III–IV). Because decreased stage III–IV sleep is seen in nocturnal bruxism<sup>13</sup> and tiagabine increases stages III–IV, this may be the mechanism by which tiagabine reduces nocturnal bruxism. It is noteworthy that an additional patient—a 48-year-old woman with severe bipolar disorder with intense, lifelong, and treatment-resistant pan-anger and anxiety—who was prescribed tiagabine did not benefit from it. Her bruxism was daytime only, and clenching

was predominant. She did not have morning jaw pain, unlike the other patients for whom tiagabine was of great relief. Her case also points to tiagabine's effect on sleep architecture as its mode of action in bruxism amelioration.

## CASE REPORTS

Patient MT was a 31-year-old woman with longstanding bipolar disorder showing exquisite rejection sensitivity and anxiety prominence. For the past 11 years she had severe morning jaw pain; her husband reported nocturnal grinding noises that would frequently awaken him. Wellbutrin (bupropion), a drug that she used to control her depressions, made these bruxism signs and symptoms markedly worse. During uptitration on successive months, tiagabine doses of 2 and 4 mg at bedtime reduced her morning jaw pain considerably (“It’s still there but not nearly the problem it was”). At a dose of 6 mg at bedtime, her jaw pain and clenching had stopped.

Patient ML was a 39-year-old man with generalized anxiety disorder that was satisfactorily treated by Lexapro (escitalopram), which neither helped nor worsened his bruxism. Clear facial asymmetry caused by massive unilateral masseter hypertrophy was present. His wife reported loud nocturnal grinding noises. Every morning for the past 8 years he had TMJ area and dental and jaw pain. Initially, 4 mg of tiagabine at bedtime was of no help in reducing some residual anxiety, but he reported good relief of pain for half the days of the week and no pain at all for the other half. After using tiagabine for several months, he reported that the TMJ area pain and bruxing sounds had stopped completely.

Patient RP was a 43-year-old woman with bipolar disorder and polycystic ovarian syndrome (PCOS) (Stein-Leventhal syndrome). She had experienced decades of jaw and facial pain with loud nocturnal grinding. Topiramate and bupropion successfully treated her mood disturbance and resulted in sufficient weight loss for remission of PCOS, but her bruxism and pain remained or worsened. She reported complete relief with the addition of 8 mg tiagabine twice daily (“It’s a miracle”).

Patient AC was a 24-year-old woman who had TMJ pain since she was an early teen and had recent onset bipolar disorder and PCOS. (There is an excess of psychiatric disorders in a PCOS population and an excess of PCOS in a psychiatric population, but an association between bruxism and PCOS is not defined.) The anticonvulsant Lamictal (lamotrigine) was of no help to TMJ area pain but was excellent in controlling her signs and symptoms of severe mood lability and periodic life-threatening depressions. She reported good reduction of morning jaw pain and nocturnal grinding with a 6-

mg dose of tiagabine at bedtime. Although mild residual bruxism was present, she wished not to pursue it with further dose increases.

## CONCLUSION

Tiagabine may be an effective treatment for nocturnal but not for daytime bruxism that remains problematic after trials of standard first-line treatments such as splints; continuous positive airway pressure (if indicated); correction of mood, anxiety, and psychosocial precipitants; and withdrawal of triggering medicines or circumstances. Formal study of tiagabine treatment of nocturnal bruxism is warranted.

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## APPENDIX

Standard sleep hygiene recommendations:

1. Have no light, fan, television, radio, or other source of light or sound. This means not having a light-emitting diode clock or any way of telling what the time is.
2. Try to keep regular hours. Go to bed at night and arise in the morning at the same time every day, including weekend days.
3. Do not use tobacco, marijuana (or other street drugs), or alcohol at any time.
4. Stop all tea, coffee, or caffeinated beverages after 3 PM.
5. If you are unable to sleep after 10 minutes or so, get up, sit elsewhere, and read. Do not watch television, listen to the radio, converse, and so on. Read alone and in silence. Go back to bed when you want to try again, but repeat the process if sleep does not come quickly.